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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/623,930

07/21/2003

Vicki Bowman Vance

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7590

05/16/2006

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EXAMINER

KUMAR, VINOD

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/623,930

Applicant(s)

VANCE ET AL.

Examiner

Vinod Kumar

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-19, 21, 22, 24 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20, 23 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/23/03; 07/30/04; 05/03/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group VI, claims 20, 23 and 26 in the paper filed on March 1, 2006 is acknowledged. Applicant's arguments filed on March 1, 2006 have been fully considered but they are not persuasive.

Applicant argue that it would not present an undue burden to search and examine claims 1-26 concurrently. In particular, it would not present an undue burden to search and examine the claims of Groups I to V and Groups VI to VIII concurrently because the claims of Groups II to V all ultimately depend from claim 1, and likewise claims of Groups VII and VIII all ultimately depend from claims 20 and 23 (in Group VI) (response, page 1, first paragraph, lines 1-14).

The examiner maintains that subject matter pertaining to the claims of Groups I-VIII is highly divergent and would impose undue search burden if the invention of any one Group were searched with the invention of any other Group, for the reasons on the record stated in Office action mailed on February 2, 2006.

Applicants further argue that search and examination of the claims of Groups I to III can be carried out without reference to a specific target sequence or modulator because these claims are drawn to methods that can be practiced with any target sequence or modulator, and the restriction to a specific target sequence or modulator reflects an unduly narrow view of the claimed invention (response, page 1, second paragraph through first paragraph of page 2). Applicants are reminded that search for

Art Unit: 1638

the invention of a Group is based on the broader scope of all the claims within that Group which must include all the recited limitations of the claims. In the instant case, searching all the species of target sequence belonging to Groups I-III would result in undue search burden for the Office. Hence, Examiner maintains that restriction requirement to a single target sequence is proper and within the meaning of § 35 USC 121. Claims 20, 23, and 26 are examined in this Office action. Accordingly, claims 1-19, 21-22 and 24-25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The non-elected subject matter must be removed from elected claims. This restriction is made FINAL.

Information Disclosure Statement

2. Initialed and dated copies of Applicant's IDS form 1449 filed on 10/23/2003, 07/30/2004 and 05/03/2005 are attached to the instant Office action.

Specification

3. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 12, line 9; page 13, line 16; page 19, line 19.

The disclosure is objected to because it fails to refer to the indicated sequences by its sequence identifier as required by 37 CFR 1.821. See page 33, line 25.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 20, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a plant cell or plant transformed with a miRNA or SiRNA precursor construct comprising a promoter operably linked with a nucleotide sequence encoding a miRNA 167 precursor sequence which comprises a sequence that is complementary to a portion of a target sequence of interest or encoding a double stranded RNA sequence comprising a portion of target sequence of interest, does not reasonably provide enablement for a plant cell or plant transformed with any RNA precursor construct operably linked to a promoter comprising any miRNA sequence that is complementary to a portion of target sequence of interest. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 20, 23 and 26 are broadly drawn to a plant cell or plant stably transformed with an RNA precursor construct, said RNA precursor construct comprising a first promoter that drives expression in a plant cell operably linked to a first nucleotide sequence encoding a precursor RNA, said precursor having at least one miRNA sequence incorporated into the precursor RNA sequence, wherein said miRNA

sequence is complementary to a portion of a first target sequence, or transformed seed of said plant.

Specification describes HC-Pro suppression of RNA silencing induced by GUS sense transgene eliminates the accumulation of SiRNAs (page 29, example 1). The specification further describes HC-Pro increases the level of miRNA accumulation in tobacco (page 30, example 2). Specification also outlines the strategies for construction and optimization of miRNA 167 precursor construct designed to target the GUS mRNA or SULFUR mRNA (pages 31-35, examples 3-6).

Claims 20 and 23 encompass any RNA precursor construct comprising at least one miRNA sequence, which has sequence complementary to a portion of a target sequence. The specification provides guidance on making SiRNA or miRNA 167 precursor constructs and using them in post-transcriptional gene silencing through transformation and expression of such precursor molecules that carry a sequence which is complementary to the target sequence. The specification provides no guidance on making RNA precursor constructs comprising RNA precursor sequences other than SiRNA or miRNA 167 which comprise a portion of a sequence that is complementary to the target sequence. For example, specification provides no guidance on making constructs comprising pre-mRNA, tRNA or rRNA precursor sequences comprising a portion of a target sequence of interest as encompassed by the claims. Furthermore, specification provides no guidance on the process of using said constructs upon transforming a plant cell or plant with said constructs. It is well established in the art of post-transcriptional gene silencing that though siRNAs and miRNAs differ in their origin, they nonetheless share similarities in their biogenesis. The precursors of siRNAs and

Art Unit: 1638

miRNAs have double stranded structures which are recognized by endogenously present processing enzyme, "dicer", to release mature miRNA or siRNA cleaved products. These small RNA species then participate in gene regulation activity including post-transcriptional gene silencing (PTGS) of a gene of interest (Bartel et al., *Plant Physiol.*, 132:709-717, 2003, Applicant's IDS; Mallory et al., *PNAS*, 99: 15228-15233, 2002, Applicant's IDS). The specification provides no guidance on how any RNA precursor other than miRNA or siRNA can form double stranded RNA molecules that is specific for dicer to cleave and release regulatory small RNA molecules. Papp et al. (*Plant Physiol.*, 132:1382-1390, 2003, Applicant's IDS) teach the existence of multiple DCL (dicer-like) enzymes involved in processing different class of short RNAs or small RNAs from double-stranded RNA precursors. For example, in *Arabidopsis*, DCL1 is required for producing miRNAs but not siRNAs. The specification does not teach the structure that the RNA precursor must have, to be recognized by the particular Dicer. Furthermore, neither the art nor the Applicants provide guidance on making pre-mRNA, tRNA, rRNA etc precursor constructs (which are encompassed by the broad recitation "RNA precursor construct"), comprising a portion of a sequence that is complementary to a target sequence. Furthermore, neither the art nor the Applicants have described the use of transforming said precursor constructs (other than siRNA and miRNA 167 precursors) into a plant cell or plant. It is highly unpredictable that any RNA precursor construct comprising a portion of target sequence when transformed into plant cell or plant will result in regulating the expression of a target gene with reasonable expectation of success. Undue experimentation is required by one skilled in the art to make and use said transformed plant cell or plant comprising said constructs

comprising RNA precursor sequence other than SiRNA or miRNA 167. Neither the state of art nor Applicant provide guidance as to how inoperable embodiments can be readily eliminated other than random trial and error. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention. Therefore, it is maintained that the claimed invention is not enabled as commensurate in scope with the claims.

5. Claims 20, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not have adequate written description for the genus of RNA precursor sequences, genus of miRNA sequences under current written description guidelines. Specification does not describe any of these sequences and one skilled in the art cannot reliably predict the structure of these sequences based upon the disclosure of miRNA 167 precursor.

Specification describes HC-Pro suppression of RNA silencing induced by GUS sense transgene eliminates the accumulation of SiRNAs (page 29, example 1). The specification further describes HC-Pro increases the level of miRNA accumulation in tobacco (page 30, example 2). Specification also outlines the strategies for construction

and optimization of miRNA 167 precursor construct designed to target the GUS mRNA or SULFUR mRNA (pages 31-35, examples 3-6).

Claims 20 and 23 encompass any RNA precursor construct comprising any miRNA sequence which has sequence complementary to a portion of a target sequence. The claims encompass structures of a broadly claimed genus whose function has not been correlated with regulating the expression of a target sequence of interest when introduced in a plant cell or plant. Applicants have failed to describe common functional domains or elements shared by these undisclosed structures. Thus, it is evident that Applicant's broadly claimed genus was not reduced to practice.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

Claim Rejections - 35 USC § 102 & 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1638

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 20, 23 and 26 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Chuang et al. (PNAS, 97:4985-4990, April 25, 2000).

Claims 20, 23 and 26 are broadly drawn to a plant cell or plant stably transformed with an RNA precursor construct, said RNA precursor construct comprising a first promoter that drives expression in a plant cell operably linked to a first nucleotide sequence encoding a precursor RNA, said precursor having at least one miRNA sequence incorporated into the precursor RNA sequence, wherein said miRNA sequence is complementary to a portion of a first target sequence, or transformed seed of said plant.

Chuang et al. teach a plant cell or plant transformed with a construct comprising a double-stranded RNA-expressing construct corresponding to a gene *AGAMOUS* (*AG*) which is involved in flower development, operably linked with a promoter and 3' terminator sequence. The stable introduction of said construct into the genome of the transgenic plant cell or plant resulted in heritable down-regulation of endogenous *AG* mRNA, suggesting that endogenous mRNA is the target of double stranded-mediated (RNA precursor) genetic interference. The reference teaches T1 and T2 progenies of

Art Unit: 1638

said transgenic plants expressing double-strand RNA precursor construct, indicating transformed seeds were produced. The RNA precursor recited in the claims reads on any type of RNA precursor including SiRNA precursor because one can not distinguish the structure of different types of RNA precursors based on the claimed invention. Furthermore, the plant taught by the reference was not made using the same method as the instantly claimed plant. However, the instantly claimed plants have the same structural limitations as that taught by the reference. See *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) which teaches that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Conclusions

7. No claims are allowed. The claims 20, 23 and 26 are not free from prior art.

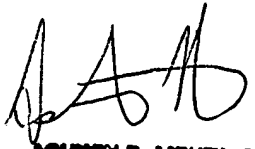
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone

Art Unit: 1638

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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PRIMARY EXAMINER